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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,249	04/04/2005	Masahiko Terakado	Q87291	9920

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EXAMINER	
MURRAY, JEFFREY H	
ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
12/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,249	TERAKADO ET AL.	
	Examiner	Art Unit	
	JEFFREY H. MURRAY	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,69-76 and 80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,69-76 and 80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1, 2, and 68 are rejected. Claims 3-67, 69-76 and 80 are withdrawn.

2. Claims 2 and 68 are pending in this application. Claim 1, 3-67 and 77-79 have been cancelled. This action is in response to the applicants' amendment after a non-final and reply filed on October 4, 2007.

Status of Objections

3. The specification was objected to for failing to properly define "Z" on page 5 within the application. The objection to the specification is hereby withdrawn in view of applicants' amendments to the specification.

4. The specification was objected to for the Abstract of the Disclosure being over the allotted 150 words maximum. The objection to the specification is hereby withdrawn in view of applicants' amendments to the Abstract of the Disclosure.

5. Claim 1 was objected to as being improper for failing to properly define "Z" in the claim. The objection to Claim 1 is moot and hereby withdrawn in view of applicants' cancellation of Claim 1.

Status of Rejections

7. Claims 1, 2 and 68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The rejection of Claims 1, 2 and 68 are hereby moot and withdrawn in view of applicants' cancellation of Claim 1 and applicant's arguments.

8. Claim 1 was rejected to as being indefinite for failing to properly define "Z" in the claim. The objection to Claim 1 is moot and hereby withdrawn in view of applicants' cancellation of Claim 1.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Election/Restrictions

9. Claim 68 is directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 69-75 and 80, directed to the process of making or using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement as set forth in the Office action mailed on January 19, 2007 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

New Rejections

Claim Rejections - 35 USC § 112, 1st paragraph

10. Claims 2, 69-76, and 80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds, compositions, and treating diseases, does not reasonably provide enablement for polymorphs, or "preventing" diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (*United States v. Teletronics* Inc., 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

These factors include the following:

1) *Unpredictability in the art*. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. (USPQ 18, 24 (CCPA 1970). See *In re Fisher*, 427 F.2d 833, 839, 166.

Morphological forms of the compound, or "polymorphs" are the ability of a substance to exist in two/more crystalline phases that have different arrangement and/or conformation of molecules in a crystal lattice.

Screening of pharmaceuticals early on in drug discovery to find out all possible solid forms has significant connotations. (Chawla et. al.; Current Research & Information on Pharmaceutical Science, 2004, 5(1), p. 9, col.2, para.1) When designing formulations, it is imperative to know which crystal form of a drug is present at the various stages of a process. "It may be possible that if one polymorph of an active pharmaceutical ingredient, or API, is responsible for activity, another form may be less active, inactive, toxic, or have some other properties of interest." (Chawla et. al.; p. 9, col.2, para.3)

Polymorphs can exhibit many types of differences in their physical properties such as a) packaging; b) thermodynamic; c) spectroscopic; d) kinetic; e) surface; and, f) mechanical properties. (Chawla et. al.; See Table 1, p. 10) These properties offer scientists the opportunity to manipulate bioavailability. It is important to determine if there are phase transformations occurring during processing as well as what crystal form is present in the final drug product. (Newman et. al.; Drug Discovery Today, 2003, 8(19) p. 898, col.2, Para.3)

The use of the term "prevention" is, unless otherwise defined, interpreted to mean inhibition of pain and inflammation once the active agent has been administered. Applicant must show that the Claimed method "prevents" pain and inflammation in a broad range of conditions. The specification fails to enable the claimed compounds for

the prevention of pain and inflammation. The term "prevention" encompasses the ability of the specific antigen to induce protective immunity to any inflammatory disorder. For example, multiple sclerosis or MS represents an unpreventable chronic illness. (Schiaffino et. al., *J.Behav.Med.*, 1995, 18(6), p.536) Chronic neurological pain is the most common and the most intractable of the pain syndromes of MS. (http://www.msakc.org/Articles/MSPain.htm). In view of the situation set forth herein, it is clear that it is not possible for the instant compounds or compositions to "prevent" pain and inflammation commensurate in scope with Claim 20.

The specification does not provide sufficient data or provide substantive evidence that the claimed compounds are capable of inducing protective immunity against urinary system diseases, carcinoma-associated diseases, proliferative diseases, inflammatory/immune system diseases or any disease referred from EDG-2 broadly. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed compound.

2) *Amount of guidance provided by Applicant*. While the Applicant has demonstrated within the application how to make the compounds of Formula IB, the applicant has not shown any useful data or guidance that would define a particular polymorph that would be biologically active. The applicant has inferred within the specification that any "morphological forms of the compound" would be acceptable. This can clearly not be the case. A contrasting example to this would be chloramphenicol palmitate (CAP). CAP exists in a form A and B. The metastable "form B" of CAP has an eight-fold higher bioactivity than "form A." Yet if "form B" is

administered to humans, it can cause potentially fatal side effects. (Chawla et. al.; p. 9-10). Also a variety of dosage forms are available for pharmaceutical products. (Newman et. al.; p. 899, col.2, Box 1) A polymorph can affect the key solid-state parameters. For example, the drug substance in a tablet formulation will be significantly different than those for an oral suspension or inhalation product. (Newman et. al.; p. 898, col.2, Para.1)

3) *Number of working examples*. Applicant has provided no detailed working examples of various polymorphs either in the crystalline or amorphous state or of any compounds or compositions that can "prevent" any of the diseases mentioned within the Claims.

4) *Nature of the invention*. The application relates to a carboxylic acid derivative having antagonisitic activity against lysophosphatidic acid receptor (especially EDG-2 receptor) which is useful as medicament, a process for producing the same and the use thereof.

5) *Level of skill in the art*. The artisan using Applicants invention would be a chemist with a Ph.D. degree, and having several years of experience or a doctor with a M.D. degree and having several years of experience.

MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)."

Conclusion

11. Claims 2, 69-76, and 80 are rejected.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is 571-272-9023. The examiner can normally be reached on Mon.-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H Murray/
Examiner, Art Unit 1624

/ James O. Wilson /
Supervisory Patent Examiner
Art Unit 1624